

Amendments to the Claims

Please cancel claims 21-45, without prejudice or disclaimer.

This listing of claims will replace all prior versions and listings of claims in the application:

Listing of Claims:

1. (Original) A method to detect a nucleotide, comprising:
 - a) restraining movement of a nucleic acid molecule attached to a single particle using a restriction barrier located within a first channel;
 - b) contacting the nucleic acid molecule with an exonuclease to release the nucleotide, wherein the nucleotide is a terminal nucleotide; and
 - c) identifying the released nucleotide by associating the released nucleotide with a surface enhanced Raman spectroscopy-active surface, irradiating the released nucleotide with a detection laser beam and measuring Raman emission from the irradiated nucleotide, thereby detecting the nucleotide.
2. (Original) The method of claim 1, wherein the restriction barrier comprises a plurality of walls.
3. (Original) The method of claim 2, wherein the restriction barrier comprises a first angled wall and a second angled wall positioned relative to the first angled wall to capture the single particle having the surface with the attached nucleic acid molecule.
4. (Original) The method of claim 1, wherein a gradient force optical trap captures the single particle downstream of the laser beam, transports the single particle upstream of the restriction barrier, and release the single particle.
5. (Original) The method of claim 1, wherein a gradient force optical trap captures the single particle downstream of the detection laser beam, the detection laser beam and the restriction

barrier are moved downstream of the captured single particle, and the single particle is released.

6. (Original) A method to determine a nucleotide sequence of a nucleic acid molecule, comprising:
 - a) restraining movement of a single particle using a restriction barrier located within a first channel, wherein the nucleic acid molecule is attached to the single particle;
 - b) contacting the nucleic acid molecule with an exonuclease to release a terminal nucleotide; and
 - c) identifying a first released nucleotide and a second released nucleotide by irradiating the first released nucleotide and then the second released nucleotide with light from a detection light source, by associating the first released nucleotide and the second released nucleotide with a surface enhanced Raman spectroscopy-active surface, and measuring Raman emission from the irradiated first released nucleotide and then from the second released nucleotide, thereby determining a nucleotide sequence of the nucleic acid.
7. (Original) The method of claim 6, wherein the restriction barrier comprises a plurality of walls.
8. (Original) The method of claim 7, wherein the restriction barrier comprises a first angled wall and a second angled wall positioned relative to the first angled wall to capture the single particle having the surface with the attached nucleic acid molecule.
9. (Original) The method of claim 6, wherein a gradient force optical trap captures the single particle downstream of the light from the detection light source, transports the single particle upstream of the restriction barrier, and releases the single particle.
10. (Original) An apparatus comprising, a first channel comprising a restriction barrier comprising a first angled wall and a second angled wall positioned relative to the first angled wall to form a first opening at least 1 micron in width or diameter and a second opening less than

10 microns in width or diameter, wherein the first opening has a greater width or diameter than the second opening.

11. (Original) The apparatus of claim 10, wherein the second opening is less than 1 micron in width or diameter.

12. (Original) The apparatus of claim 10, further comprising a light source and a detector to detect a surface enhanced Raman spectroscopy emission of a molecule irradiated by the light source, the first channel in optical communication with the light source and the detector.

13. (Original) A system comprising:

- a) a light source;
- b) a detector to detect a surface enhanced Raman spectroscopy emission of a molecule irradiated by the light source; and
- c) a first channel in optical communication with the light source and the detector, wherein the first channel comprises a restriction barrier comprising a plurality of walls to restrain movement of a single particle upstream of light emitted by the light source.

14. (Original) The system of claim 13, wherein the restriction barrier comprises a first angled wall and a second angled wall positioned relative to the first angled wall to form a first opening at least 1 micron in width or diameter and a second opening less than 10 microns in width or diameter, wherein the first opening has a greater width or diameter than the second opening.

15. (Original) The system of claim 14, further comprising a laser light source and a series of lenses to form a gradient force optical trap.

16. (Original) The system of claim 15, further comprising a second channel forming a junction with the first channel.

17. (Original) The system of claim 16, wherein the restriction barrier is located upstream of the junction of the first channel and the second channel.

18. (Original) The system of claim 17, wherein the gradient force optical trap is positioned downstream of the junction of the first channel and the second channel.

19. (Original) The system of claim 18, wherein the light source is positioned downstream from the restriction barrier and upstream from the gradient force optical trap.

20. (Original) The system of claim 13, wherein a portion of a flow path in optical communication with the detection light source is coated with silver, gold, platinum, copper or aluminum.

Claims 21-45 canceled.